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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,433	08/16/2001	Luc Aujame	P07180USOO/BAS	7146

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	16

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/830,433	Applicant(s) AUJAME ET AL.	
	Examiner Padmavathi v Baskar	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,10 and 14-24* is/are pending in the application.

4a) Of the above claim(s) *1,3-6,10,14 and 16, 18, 20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,17,19,21,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

1. Applicant's amendment filed on 7/8/03 (paper # 15) is acknowledged. Claims 2, 7, 8 and 11-13 have been canceled. New claims 15-24 have been added. Claims 1, 3-6, 10 and 14 are withdrawn from consideration as non-elected invention. The newly added claims 15, 17,19, 21 23 and 24 read on the previously prosecuted invention (claims drawn to an isolated nucleic acid SEQ.ID.NO: 7 which encodes SEQ.ID.NO: 8). Claims 16, 18, 20, 22 are not drawn to elected sequence (SEQ.ID.NO: 53 is not an elected SEQ.ID.NO). Therefore, claims 16, 18, 20, 22 are not considered as an elected invention and are withdrawn from consideration. Claims 15, 17;19, 21, 23 and 24 with respect to SEQ.ID.NO: 8 are under examination.

2. In view of cancellation of the prosecuted claims 2,7,8 and 11-13, all the rejections of record are moot.

3. The examiner acknowledges the abstract submitted. It has been placed in the application.

Claim Rejections - 35 U.S. C. § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 15, 17,19, 21, 23 and 24 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. This is a written description rejection.

The specification broadly describes as part of the invention the sequence of the open reading frame derived from *Neisseria* strain ATCC13090 is SEQ.ID.NO: 7 and the amino acid sequence in deduced form is SEQ.ID.NO: 8 (pages 3-5). The specification also broadly describes their novel polynucleotide sequence of SEQ ID NO: 7. The actual biological function of the polypeptide encoded thereby and represented as SEQ ID NO: 8 is not set forth in this specification. Applicants also broadly describe the invention as embracing any substitution, insertion or deletion change of nucleotides throughout the entire stretch of nucleotides found in the encoding or reference sequence by use of language in which a specified percent of amino acid 80%-95% identity to SEQ.ID.NO: 8 or antigenic fragments can be made in the polypeptide. None of the polypeptides as claimed meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116.).

The specification only discloses a polynucleotide sequence SEQ ID NO: 7 encoding the protein SEQ ID N0: 8 from Neisseria species. Thus, an isolated polynucleotide encoding the amino acid SEQ ID NO: 8 meet the written description provision of 35 U.S.C. 112, first paragraph for the reasons set forth below.

The specification fails to teach antigenic fragment of a polypeptide sequence of SEQ ID NO: 8 and it is noted that the claimed fragments do not exist as an invention independent of

their function in encoding a protein. The actual structure or other relevant identifying characteristics of each nucleic acid that encodes an antigenic fragment i.e. 80-95% having the claimed properties of the protein can only be determined empirically by actually making every nucleic acid that encodes the recited variability (i.e. the instant 80%-95% identity) and testing each to determine whether it encodes a protein having the antigenic properties of an isolated polypeptide specific for pathogenic Neisseria strain. The isolated nucleic acid, which encodes antigenic fragments, is uncharacterized by this specification and is not asserted to belong to any known family of proteins. The specification fails to teach the structure or relevant identifying characteristics of antigenic fragment or polynucleotides encoding such antigenic fragments as claimed, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. With the exception of an isolated polynucleotide comprising the nucleic acid SEQ ID NO: 7 and an isolated polynucleotide comprising the nucleotide sequence encoding SEQ ID NO: 8, fragments thereof have not been disclosed. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chugai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483.

6. Claims 15, 17,19, 21, 23 and 24 are rejected under 35 U.5.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid which encodes the polypeptide SEQ ID NO: 8, vector and host cell comprising said nucleic acid, the specification does not reasonably provide enablement for an isolated nucleic acid which encodes a polypeptide comprising 80%, 90% and 95% sequence identity with the amino acid sequence as shown in SEQ.ID.NO: 8 or antigenic fragments thereof, vectors comprising the said nucleic acids, host cells. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to and encompass polynucleotides, which comprise a nucleotide sequence, which has a recited percent identity (80%-95%) with SEQ ID NO: 8 or antigenic fragments thereof and vectors and host cells. These claims are not enabled for the following reasons. The written description is limited to only SEQ ID NO: 8 which is the corresponding amino acid sequence encoded by the polynucleotide, SEQ ID NO: 7. The specification fails to indicate that the biological activity of SEQ ID NO: 8 and fails to teach that SEQ ID NO: 8 is detected by immune or convalescent sera and further lacks any description of any antigenic fragments or any polynucleotide which encode such fragments that can bind to full-length protein. The specification is not enabled for any antigenic fragments or an isolated nucleic acid sequence which encodes a 80-95% identical polypeptide, because 1) the specification fails to teach that the alleged nucleic acid molecule that encodes 80-95% polypeptide of SEQ ID NO: 8 or antigenic fragments are able to function as a diagnostic by binding immune sera from convalescent patients; 2) the specification fails to teach how to make and use nucleic acid sequences which encode proteins or variants thereof that have an unknown and uncharacterized function; 3) the specification fails to teach what are the critical nucleic acid and protein residues that can be modified and still achieve a nucleic acid encoding a protein with any functional activity or any variant nucleic acid diagnostic characteristics or any nucleic acid with immunogenic/pharmaceutical/vaccine characteristics for pathogenic Neisseria, 4) the art teaches that proteins with replacement of single amino acid residues may lead to both structural and functional changes in biological activity and immunological recognition, one skilled in the art would have reason to doubt the validity and functionality of the function of the protein of SEQ ID

NO:8 and 5) applicants have not displayed a nexus between the structure of the polynucleotide sequence and function of the polypeptide as claimed.

As to points 1)- 5), the specification fails to provide a written description of any antigenic fragments of the bacterial protein sequence of SEQ ID N0: 8 and the corresponding encoding polynucleic acids, which function equivalently to a polypeptide comprising the disclosed SEQ ID NO: 8. The specification fails to teach the critical protein residues involved in the function of the protein SEQ ID NO: 8 such that the skilled artisan is provided guidance to test, screen or make such fragments or variants with 80%-95% sequence identity, using conventional technology which allow for a screening or diagnostic use in the specification. In order to be diagnostic the sequence must distinguish pathogenic from non-pathogenic Neisseria sp. and other clinically relevant bacteria in a host. The specification also fails to demonstrate the actual biological function of the DNA and protein and only assigns it a putative characteristic as a pathogenic protein. Even if one were to use the methodology of the specification to screen for antigenic fragments or variants, one of skill in the art would be reduced to merely randomly altering nucleic acids and amino acid(s) which would lead to unpredictable results regarding the functional activity of the DNA encoding protein and the ability of the nucleic acid to be used as a vaccine. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted a priori and must be determined empirically on a case by case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin

binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a protein. Proteins with replacement of a single amino acid residue may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis in proteins that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. Applicants have not taught which residues of SEQ ID NO: 8 can be varied and still achieve a protein that is functional. Since, the specification lacks a written description of any antigenic fragment of SEQ ID NO: 8 or polypeptide with % identity to SEQ ID NO: 8, it is not enabled for this language because it fails to enable the skilled artisan to envision the detailed I structure of the claimed polynucleotide encoding antigenic fragments of SEQ ID NO: 8. One of skill in the art would be unable to produce these polynucleotides encoding antigenic fragments or polynucleotide variants (80-95% sequence identity) encompassed by the instant claims. Further, if one nucleotide is deleted or inserted at a single place within the coding sequence, all the codons down stream of that insertion or deletion will be frame shifted. If that frame shift takes place near the 5' end of the gene, it is highly likely that the protein expressed will have little in common structurally or functionally with the protein. In this regard, applicant has not enabled the

scope of the invention as claimed. The specification discloses a novel Neisseria protein and a nucleic acid encoding it. Therefore, such undisclosed and unidentified nucleic acids which result from these, insertions, deletions or substitutions encompasses by the recited "80% - 95% identical" to an polypeptide encoded by an undefined reading frame from SEQ ID NO: 8 are not enabled for their scope. The skilled artisan would be forced into undue experimentation to make and use the instantly claimed scope of invention.

Claim rejection under 35 U.5.C. 112, second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 15, 17,19, 21, 23 and 24 are rejected under 35 U.5.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 15, the claim is indefinite because the claim recites that an isolated polynucleotide sequence which encodes a polypeptide ----. However, an isolated polynucleotide has minimum 6 reading frames, each encoding its own distinct polypeptide. Therefore, the metes and bounds of the claimed nucleic acid is unclear.

Status of Claims

9. No claims are allowed.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP ' 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

9/16/03

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